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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/613,359	07/03/2003	Per O. Ljungdahl	NY-LUD 5839-US	7240

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EXAMINER	
FIELD, TAMMY K	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/613,359	LJUNGDAHL ET AL.	
	Examiner	Art Unit	
	Tammy K. Field	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *13 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/02/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, Claims 1-12 received in the Office March 22, 2004 is acknowledged. Responsive to Applicants request for clarification of point 3 in the Office Restriction, point 3 is withdrawn as the rejoinder of product and method claims does not apply to Applicants instant application.

2. Claims 13-14 are withdrawn from examination as being drawn to the non-elected group of invention and Claims 1-12 are currently under examination.

Specification

The disclosure is objected to because of the following informalities:

a. There appears to be a typo at page 16, paragraph 81, "*Schizosoccharmoyces*". Does applicant intend to disclose *Schizosaccharomyces* fungal infection?

b. The specification has not been checked to the extent necessary to determine the presence of all possible minor spelling and grammatical errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Appropriate correction is required.

Oath/Declaration

3. Under Foreign Priority Papers heading, it appears that priority is claimed as "Yes", indicated by the "(X)", but there appears to be no identification of such priority papers. For the purposes of examination, the Office will proceed with examination using the effective filing date of July 3, 2000 as the priority date.

Information Disclosure Statement

The information disclosure statement(s) filed October 2, 2003 has been considered. An initialed copy is enclosed.

Claim Objections

4. Claim 10 is objected to because of the following informalities:

c. There appears to be a typo, "*Schizosoccharmoyces*". Does applicant intend to claim *Schizosaccharomyces* fungal infection? Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims encompass a method for screening for an agent useful in treating a fungal infection, more specifically *Candida* sp. and *Candida albicans*, Schizosoccharomyces, Aspergillus, Botyrotinia, and Neurospora infections, comprising contacting a fungal sample with

a compound for antifungal activity testing and determining activity of a Csh3p a Csh3p analog, a nucleic acid molecule encoding Csh3p or a nucleic acid molecule encoding a CsH3p analog. Subsequent claims encompass the activity of Csh3p or Csh3p analog; virulence, hyphal formation, and amino acid uptake and, wherein said fungal sample is heterozygous for Csh3p or Csh3p analog and homozygous recessive for Csh3p or Csh3p analog, and wherein infection is a human infection and infestation of an agricultural crop.

Biological deposits of *C. albicans* strains of CSH3 wild type fungi including mutant strains thereof, *e.g.* PMRCA18, PMRCA19, PMRCA12, and PMRCA13 for screening for an agent useful in treating a fungal infection with a compound for testing antifungal activity and determining activity of a "Csh3p a Csh3p analog, a nucleic acid molecule encoding Csh3p or a nucleic acid molecule encoding a CsH3p analog" are required to practice the claimed invention because the fungal strains of wild type and mutants appear to be vital elements of the instant invention and without such deposits, one of skill in the art would be unable to make and use the invention as claimed. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of fungal strains of wild type and mutants. See 37 CFR 1.802. One cannot practice the claimed invention without said fungal strains. Therefore, access to said fungal strains is required to practice the invention. The specification does not provide a repeatable method for readily identifying said fungal strains without access to said fungal strains and it does not appear to be readily available material.

Deposit of *C. albicans* fungal strains of the instant invention in a recognized deposit facility would satisfy the enablement requirements of 35 U.S.C. 112, because the strains would be readily available to the public to practice the invention claimed, see 37 CFR 1.801- 37 CFR 1.809. If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;
(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;
(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and
(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

6. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims encompass a method for screening for an agent useful in treating a fungal infection, more specifically *Candida* sp. and *Candida albicans*, Schizosoccharomyces, Aspergillus, Botyrotinia, and Neurospora infections, comprising contacting a fungal sample with a compound for antifungal activity testing and determining activity of a Csh3p a Csh3p analog, a nucleic acid molecule encoding Csh3p or a nucleic acid molecule encoding a CsH3p analog. Subsequent claims encompass the activity of Csh3p or Csh3p analog; virulence, hyphal formation, and amino acid uptake and, wherein said fungal sample is heterozygous for Csh3p or Csh3p analog and homozygous recessive for Csh3p or Csh3p analog, and wherein infection is a human infection and infestation of an agricultural crop.

The teachings of the specification disclose the methodology of the instant invention can be (emphasis added) used to identify useful antifungal agents and that such agents can be (emphasis added) inhibitors of Csh3p or homologs or inhibitors of expression of Csh3p corresponding genes. It appears that a "Csh3p or Csh3p analog" sequence(s) is/are not disclosed in the instant specification. Thus, it is unclear as to the genetic relatedness of Shr3p in *S. cerevisiae* to Csh3p in *C. albicans*? As to Example 1, what is the sequence of CSH3 and where in the fungal genome is at least one CSH3 allele deleted? What is the sequence of the 1.7kb fragment and how does it correspond to the allele of CSH3 in contig 19-1017? What is the sequence containing an amino acid change at position 213? What is the sequence of pPM57?

As to Example 2, where is the CA14 strain deposited? What is the sequence of the CSH3-GFP fusion protein? As to Example 3, where is the FGY145 strain deposited? As to Example 4, where is the PMCR8 and PMRCA10 strains deposited? As to Examples 5, 8, and 10, where are the biological isolates of PMRCA18, PMRCA19, PMRCA12, and PMRCA13 deposited? What are the genotypes of the yeast mutants and where are the mutations located? How does Example 7 relate to instant Claims 8 and 9? As to Example 9, what are the sequences of csh3 null mutants including (-/-) and wild type strain of (+/+)? It is unclear how the addition of proline is useful in screening agents useful in treating a fungal infection? Further, as disclosed in Example 10, how is virulence of various strains measured by administering mutated strains of *C. albicans* in BALB/c mice useful in treating a fungal infection in a human and agricultural crop infestation? How is the homolog Psh3p in *Schizosoccharomyces pombe*, *Aspergillus nidulans*, *Botyrotinia fuckelinia*, and *Neurospora carssa* related genetically to Shr3p and Csh3p? It is further unclear what therapeutic agents are useful for treating fungal infections?

Borisy, A.A. *et al.* 2003. (PNAS 100(13): 7977-7982 teach methods for screening small molecule agents useful in treating fungal infection of *C. albicans* using proliferation, colony-forming, and dye efflux assays (see Methods).

In view of the state of the art set forth supra, there appears to be a lack of direction present in the specification providing sufficient guidance for one of skill in the art to practice the instant invention using Csh3p inhibitors in treating either a human infection or an infestation of an agricultural crop. Further, without working examples providing one of skill in the art access to the strains of fungus disclosed for treating fungal infections using "Csh3p a Csh3p analog" of

the fungal strains, one of skill in the art would be unable to make and use the invention as claimed.

7. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims encompass a method for screening for an agent useful in treating a fungal infection, more specifically *Candida* sp. and *Candida albicans*, Schizosoccharomyces, Aspergillus, Botyrotinia, and Neurospora infections, comprising contacting a fungal sample with a compound for antifungal activity testing and determining activity of a Csh3p a Csh3p analog, a nucleic acid molecule encoding Csh3p or a nucleic acid molecule encoding a CsH3p analog. Subsequent claims encompass the activity of Csh3p or Csh3p analog; virulence, hyphal formation, and amino acid uptake and, wherein said fungal sample is heterozygous for Csh3p or Csh3p analog and homozygous recessive for Csh3p or Csh3p analog, and wherein infection is a human infection and infestation of an agricultural crop.

The specification discloses the nucleic acid sequences of primers used for cloning CSH3, which is the C. albicans homolog of the *S. cerevisiae* packaging chaperone, Shr3p at page 4, paragraph 13. The specification appears to be silent as to the sequence listing of DNA isolated from *C. albicans* SC5314, heterozygous for Csh3p or Csh3p analog, and homozygous recessive for Csh3p or Csh3p analog that appears to be vital to making and using Applicants claimed invention. Further, it is unclear if/how Andreasson, C. *et al.*'s incorporation by reference in its

entirety at page 17 relates to the instant disclosure of a CSH3/csh3Δ mutant, PMCRA8, and a homozygous csh3Δ/csh3Δ mutant, PMCRA10 beginning at page 7 in Example 4, and csh3, csh3Δ mutants beginning at page 8 in Example 5, and CSH3-GF fusion protein.

Andreasson, C. *et al.* 2002. (Genes & Develop. 16: 3158-3172) teach specifically defined regions of DNA in STP1 in Results and Fig. 1C of the ASI13-1 allelic mutation that defines an inhibitory domain within the stp1p. Andreasson, C. *et al.* futher teach sequences comprising the direct nucleotide repeats in the STP1 identifying specific relatedness of alignments, *i.e.* nucleotides 1-39 and 175-213 and matching base pairs in addition to identifying specific sequences removed in the STPΔ131 deletion allele.

In view of the state of the prior art set forth supra and/or full scope of Applicant's claimed invention, it would require undue experimentation by one of skill in the art to practice the invention as claimed. Without additional direction or guidance provided by the inventor disclosing the amino acid sequences of "Csh3p a Csh3p analog, a nucleic acid molecule encoding Csh3p or a nucleic acid molecule encoding a Csh3p analog", and providing identification of specific SEQ ID: #s relating to nucleic acid and/or amino acid sequences thereof, one of skill in the art would be unable to apply a method for screening for an agent useful in treating a fungal infection.

8. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The language of the claims is not as precise as the subject matter permits such that one may reasonably know the metes and bounds of the claimed subject matter. The claims are

indefinite in the recitation of "Csh3p a Csh3p analog", "a nucleic acid molecule encoding Csh3p" or "a nucleic acid molecule encoding a Csh3p analog" because it is unclear from the specification what applicant intends. Clarification is required in order to overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

9. Claims 1-7, 10-11 are rejected under 35 U.S.C. 102(a) as being anticipated by Borisy, A.A. *et al.* 2003. (PNAS 100(13): 7977-7982).

The claims encompass a method for screening for an agent useful in treating a fungal infection, more specifically *Candida* sp. and *Candida albicans*, Schizosoccharomyces, Aspergillus, Botyrotinia, and Neurospora infections, comprising contacting a fungal sample with a compound for antifungal activity testing and determining activity of a Csh3p a Csh3p analog, a nucleic acid molecule encoding Csh3p or a nucleic acid molecule encoding a CsH3p analog. Subsequent claims encompass the activity of Csh3p or Csh3p analog; virulence, hyphal formation, and amino acid uptake and, wherein said fungal sample is heterozygous for Csh3p or Csh3p analog and homozygous recessive for Csh3p or Csh3p analog, and wherein infection is a human infection and infestation of an agricultural crop.

Borisy, A.A. *et al.* teach a method for screening for an agent useful in treating fungal infections by proliferation assay using stock solutions of compounds, *i.e.* agents, wherein *C. albicans* is seeded in 384-well plates containing growth medium, small molecular weight compounds that perturb cellular signaling networks and testing viable cells of *C. albicans* (inherently only live *C. albicans* cells are able to be virulent and have biological activity, specifically hyphal formation and amino acids uptake) at paragraph 1 and Methods, pages 7977-7978.

Thus, Borisy, A.A. *et al.* Anticipates the instantly claimed invention.

10. Since the office does not have the facilities for examining and comparing applicants' detection and diagnosis methods with the methods disclosed in the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed method and the methods of the prior art (*i.e.* that the methods of the prior art does not possess the same material structural and functional characteristics of the claimed methods). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald *et al.*, 205 USPQ 594.

Status of the Claims

11. No claims allowed.

Conclusion

12. The prior art of record and not relied upon is considered pertinent to applicant's disclosure:

d. Surber, *et al.* US PreGrant Patent Application Publication 2003/0224369 A1 published December 4, 2003 with prior filing date of May 28, 2002.

e. Lalgudi, *et al.* US PreGrant Patent Application Publication 2001/0051335 A1 published December 13, 2001 with prior filing date of April 16, 1999.

f. Setterstrom, *et al.* US Patent 6,309,669 B1 issued October 30, 2001.

g. Melnick, *et al.* US Patent 4,311,794 issued January 19, 1982.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tammy K. Field whose telephone number is (571) 272-0856. The examiner can normally be reached on Monday-Friday from 7am-4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached at (571) 272- 0864.

Papers relating to this application may be submitted to Technology Center 1600 Group 1640 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306 for regular communications and After Final communications.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov./. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

TKF

Tammy K. Field
April 5, 2004

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